Scientific abstract

Title: Phase II Trial of Surgery with Perioperative RPR/INGN 201 (Ad5CMV-p53) Gene Therapy Followed by Chemoradiotherapy for Advanced, Resectable Squamous Cell Carcinoma of the Oral Cavity and Oropharynx (S0011).

This phase II study will assess the feasibility of treating newly diagnosed stage III and IV squamous cell carcinoma of the oral cavity and oropharynx with perioperative RPR/INGN 201 gene therapy along with surgery and chemoradiation in a multi-institutional setting. The secondary objectives are 1) To assess added toxicity of perioperative RPR/INGN 201 and 2) To assess time until progression, time to local relapse, and overall survival.

In the proposed trial, we are planning to transduce *p53* in tumor and preneoplastic foci within the surgical microenvironment to induce apoptosis in order to improve local control. The safety and antitumor activity demonstrated in Phase I and II trials have led us to develop this perioperative Phase II trial. In the single-center phase I trial, a cohort of 15 patients that had recurrent & refractory cancer and were eligible for palliative surgical resection were enrolled (Clayman et al, 1998, *J.Clin.Oncol.* 2221-32; Clayman et al, 1999, *Clin.Cancer Res*, 1715-22). Patients underwent a surgical resection and were given an intraoperative injection of Ad-p53 in the resected tumor bed and in the neck dissection site. Three days later, their drainage catheters were injected (retrograde) with Ad-p53. This perioperative approach was found to be safe and well tolerated with no significant added wound complications.